REMARKS

With entry of this amendment, claims 35, 37-40 and 42-51 are pending. Claims 1-34, 36, and 52-57 are cancelled, without prejudice, to advance examination of certain aspects of the invention.

Double Patenting and Rejections Under 35 U.S.C. § 103

Claims 35, 37-40 and 42-51 are rejected under the judicially created doctrine of obviousness-type double patenting over Patent No. 6,814,962, and under 35 U.S.C. §103 over WO 96/11276, in view of Kozaki et al as evidenced by Gotada et al.

In the context of the objections, claims 2 and 5 of the '962 patent are identified as being directed to the administration of a viral gene therapy vector to administer an amount of LPL protein that would be effective to reduce triglyceride levels in the patient. The specification of the '962 patent is relied on for teachin g that decreased catalytic activity of lipoprotein lipase results in lower HDL-C levels and higher triglyceride levels (particularly the paragraph bridging columns 2-3, the Abstract, and page 2, lines 21-22). It is asserted that the cited art would therefore lead one to expect the administration of the viral gene therapy vector, as claimed in the '962 patent, to result in a decrease in triglycerides, as claimed, as well as an increase in HDL-C. Kozaki et al. is relied upon for teaching that the S447X truncation of LPL is a functional variant that has a specific activity twice that of wild type LPL. On this basis, the decrease in triglycerides and increase in HDL-C resulting from the expression of an LPL protein including the S447X LPL protein is characterized as not an unexpected result.

With respect to the necessary inquiry into the scope and content of the prior art, it is respectfully submitted that the teachings of Kozaki et al. in particular must be viewed in the context of additional references. In particular, Kozaki et al also teach (in the paragraph bridging pages 1770 and 1771) that contradictory results have been published concerning the effect of the S447X truncation on LPL activity. In particular, Kozaki et al refer to Faustinella et al (identified as reference 10) reporting that the S447X truncation has no effect on LPL activity in vitro, i.e. neither an increase or decrease of activity as compared to wt-LPL. Faustinella et al. further report, on the basis of human genomic screening, that "the Ser^{447} -> Ter mutation...is a sequence polymorphism of no functional significance." In contrast, Kobayashi et al (referred to as

reference 29) report that the S447X truncation when expressed in vitro results in a reduction of LPL activity that is 45% of wt-LPL. Kobayashi et al. in fact suggest that the truncation is pathological, in the sense that it is suggested that it might be "responsible for the property of the LPL with a defect in lipid interface recognition in the type I patient". In the face of this contradictory evidence, Kozaki et al. end the paragraph at page 1771 with the conclusion "(b)ut further studies are required to show the effect of the Ser447 stop mutation."

In contrast to the type of data and the nature of the results in all three of Kozaki et al, Faustinella et al and Kobayashi et al, the present application provides surprising results from animal models. In particular, Example 1 establishes that wt LPL **was not** effective to treat the mouse model of complete LPL deficiency, whereas the LPL-S447X variant **was** effective. This is particularly relevant with respect to claim 37. Furthermore, Examples 2 and 5 of the application also show **dramatic** difference between treatment with wt LPL and treatment with the LPL-S447X variant in mouse models that do not have a complete LPL deficiency: +/- LPL in Example 2 and -/- ApoE in Example 5. In present Example 2 (as disclosed on page 30, lines 5-6 of WO 01/00220) there was a significant increase in both HDL-C and total-C only in the Ad-447 group. At the same dose, in the Ad-LPL cohort, there was a slight **decrease** in HDL-C.

There is no teaching in the cited references upon which one skilled in the art could form a reasonable expectation of success in using a viral vector to deliver an amount of S447X therapeutic effective to lower triglycerides **and** to raise HDL-C in patients suffering from hyperlipidemia associated with LPL or ApoE deficiency. It is respectfully submitted that the showing of unexpected results in the application itself, particularly Examples 1, 2 and 5, is more than sufficient to overcome a *prima facie* case of obviousness (see, e.g., *In re Albrecht*, 514 F.2d 1389, 1396, 185 USPQ 585, 590 (CCPA 1975)).

Conclusion

The applicants submit that the claims are in condition for allowance and respectfully request that a timely Notice of Allowance be issued in this case.

September 18, 2008

Respectfully Submitted,

BLACK LOWE & GRAHAM PLLC

/S/

Jeffrey J. King, Esq.
Registration No. 38,515
Black Lowe & Graham PLLC
701 Fifth Avenue – Suite 4800
Seattle, WA 98104
Telephone: (206) 381-3300
Facsimile: (206) 381-3301